

AMENDMENTS TO THE SPECIFICATION:

Please replace paragraph 27, on page 9, with the following:

Figure 2(A) and 2(B) are ~~is-a~~ corresponding view highlighting a protein peak at about 4780 Da in CJD-infected CSF samples;

Please replace paragraph 28, on page 9, with the following:

Figure 3(A) and 3(B) are ~~is-a~~ corresponding view highlighting protein peaks at about 6700 and 8600 Da in CJD-infected CSF samples;

Please replace paragraph 29, on page 9, with the following:

Figure 4(A) and 4(B) are ~~is-a~~ are corresponding view highlighting a protein peak at about 13375 Da in CJD-infected CSF samples;

Please replace paragraph 31, on page 9, with the following:

Figure 6(A) and 6(B) are ~~is-a~~ views corresponding to Figure 5 and highlighting a protein peak at about 10220 Da in BSE-infected plasma samples;

Please replace paragraph 33, on page 9, with the following:

Figures ~~8A and 8B~~ 8(A) - 8(D) are views corresponding to Figure 7 and highlighting polypeptide peaks that are differentially expressed in the CJD+ and CJD- plasma samples;

Please replace paragraph 34, on page 9, with the following:

Figures ~~9A to 9E~~ 9(A) - 9(O) are spectral views of plasma from CJD-infected patients (plasma CJD) and non-infected patients (plasma CTS) highlighting further polypeptide peaks that are differentially expressed in the infected and non-infected samples.

Please replace paragraph 35, on page 10, with the following:

Figures ~~10A to 10F~~ 10(A) - 10(L) are spectral views of plasma from normal and BSE-infected samples using laser desorption/ionization mass spectrometry, highlighting protein peaks at about 1010, 1100, 1125, 1365, 3645, 4030, 3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and 31800 Da in plasma samples;

Please replace paragraph 59, on page 17, with the following:

Figures 1 to 4 show the results of a comparative study which has been undertaken between CSF from CJD-diagnosed patients and normal CSF, using the IMAC 3 protein chip array prepared as described above. In this study, we found that four peaks were significantly differentially increased in CSF from CJD-affected patients. Their molecular weights are respectively about 4780, 6700, 8600 and 13375 (mass accuracy is around 0.1%). Figure 1 shows two spectral views, respectively, of the normal and CJD sample, from 0 to 100,000 Da. ~~Figure-2~~ Figures 2 (A) and 2(B) show the protein peak of 4780 Da, ~~Figure-3~~ Figures 3(A) and 3(B) show the protein peaks of 6700 and 8600 Da, and ~~Figure-4~~ Figures 4 (A) and 4(B) show the protein peak of 13375 Da. These data demonstrate that the peaks of about 4780, 6700, 8600 and 13375 Da can be used to diagnose CJD in CSF samples.

Please replace paragraph 60, on page 17, with the following:

Example 1 was repeated using plasma samples from BSE-infected cattle (BSE+) and non-infected cattle (BSE-). The results are shown in Figures ~~5 and 6~~ 5, 6(A) and 6(B). Figure 5 shows a spectral view of each kind of sample from 0 to 50,000 Da. We observed that a protein around 10220 Da was significantly increased in BSE+ plasma samples, as illustrated in ~~Figure 6~~ Figures 6(A) and 6(B). This demonstrates that the peak of about 10220 Da can be used to diagnose BSE in plasma samples.

Please replace paragraph 61, on page 17-18, with the following:

Example 2 was repeated using plasma samples from CJD-infected patients (CJD+) and non-infected patients (CJD-, also referred to as CTS = Swiss Transfusion Centre). The results are shown in Figures 7 and 8. Figure 7 shows a spectral view of each kind of sample from 0 to 50,000 Da. We observed that polypeptides of about 3970, about 3990, about 4294, about 4478, about 10075, about 11730, about 14043 or about 17839 were significantly decreased in CJD+ plasma samples, as illustrated in ~~Figure 8~~ Figures 8(A) – 8(D). We also observed that a peak of about 7770 Da was increased in CJD+ plasma samples, as illustrated in ~~Figure 8~~ Figures 8(C) – 8(D). This demonstrates that the peak of about 3970, about 3990, about 4294, about 4478, about 10075, about 11730, about 14043, about 17839 or about 7770 Da can be used to diagnose CJD in plasma samples.

Please replace paragraph 63, on page 18, with the following:

In ~~Figure 9A~~ Figures 9(A)-9(C), the arrow indicates a peak at about 3295 Da, which is decreased in the CJD samples.

Please replace paragraph 64, on page 18, with the following:

In ~~Figure 9B~~ Figures 9(D)-9(F), the arrows in order from the left-hand side show the following:

1 - a peak at about 3976 Da, which is decreased in the CJD samples
(corresponding to the 3970 Da peak in Example 3)

2 - a peak at about 3992 Da, which is decreased in the CJD samples
(corresponding to the 3990 Da peak in Example 3)

3 - a peak at about 4300 Da, which is decreased in the CJD samples
(corresponding to the 4294 Da peak in Example 3)

4 - a peak at about 4315 Da, which is decreased in the CJD samples

5 - a peak at about 4436 Da, which is decreased in the CJD samples

6 - a peak at about 4484 Da, which is decreased in the CJD samples
(corresponding to the 4478 Da peak in Example 3)

Please replace paragraph 65, on page 19, with the following:

In ~~Figure 9C~~ Figures 9(G)-9(I), the arrow indicates a peak at about 6200 Da, which is decreased in the CJD samples.

Please replace paragraph 66, on page 19, with the following:

In ~~Figure 9D~~ Figures 9(J)-9(L), the arrows in order from the left-hand side show the following:

10 - a peak at about 7574 Da, which is increased in the CJD samples

11 - a peak at about 7773 Da, which is increased in the CJD samples
(corresponding to the 7770 Da peak in Example 3)

12 - a peak at about 7930 Da, which is increased in the CJD samples

13 - a peak at about 7975 Da, which is increased in the CJD samples

14 - a peak at about 8020 Da, which is increased in the CJD samples

15 - a peak at about 8936 Da, which is decreased in the CJD samples

16 - a peak at about 9107 Da, which is decreased in the CJD samples

17 - a peak at about 9145 Da, which is decreased in the CJD samples

18 - a peak at about 9185 Da, which is decreased in the CJD samples

19 - a peak at about 9454 Da, which is decreased in the CJD samples

Please replace paragraph 67, on pages 19-20, with the following:

In ~~Figure 9E~~ Figures 9(M)-9(O), the arrows in order from the left-hand side show the following:

20 - a peak at about 10068 Da, which is decreased in the CJD samples
(corresponding to the 10075 Da peak in Example 3)

21 - a peak at about 13550 Da, which is decreased in the CJD samples

22 - a peak at about 17809 Da, which is decreased in the CJD samples
(corresponding to the 17839 Da peak in Example 3)

Please replace paragraph 72, on page 22, with the following:

~~Figures 10A-10F~~ 10(A)-10(L) show the results of a comparative study, which has been undertaken between plasma from BSE-diagnosed cattle and normal plasma, using the IMAC3 protein chip array prepared as described above. In this study, we found that 23 peaks were

significantly differentially expressed in plasma from BSE-affected cattle. Their molecular weights are, respectively, about 1010, 1100, 1125, 1365, 3645, 4030, 3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and 31800 Da (mass accuracy is around 0.1%). ~~Figure 10~~ Figures 10(A)-10(L) shows two spectral views, respectively, of the normal and BSE samples, from 0 to 100,000 Da. More specifically, as indicated by the vertical arrows, ~~Figure 10~~ Figures 10(A) and 10(B) shows the peaks at about 1010, 1100, 1125 and 1365. ~~Figure 10B~~ Figures 10(C) and 10(D) shows the peaks at about 3645 and 4030. ~~Figure 10C~~ Figures 10(E) and 10(F) shows the peaks at about 3890, 5820, 7520, 7630 and 7980. ~~Figure 10D~~ Figures 10(G) and 10(H) shows the peaks at about 9950, 10250, 11600 and 11800. ~~Figure 10E~~ Figures 10(I) and 10(J) shows the peaks at about 15000, 15200, 15400, 15600 and 15900. ~~Figure 10F~~ Figures 10(K) and 10(L) shows the peaks at about 30000, 31000 and 31800.

Please replace paragraph 73, on page 23, with the following:

Spectra P1 to P20 (~~Figures 10A-10B~~ 10(A)-10(D)) correspond to a batch of samples from UK, and spectra 1 to 20 (~~Figures 10C-10F~~ 10(E)-10(I)) correspond to a batch of samples from US. The status of the cattle providing the samples is indicated below in Tables 1 and 2, where negative means not affected by BSE and positive means BSE-affected cattle.

Table 1		
#	Type	Status
P1	Plasma	Negative
P2	Plasma	Negative
P3	Plasma	Positive
P4	Plasma	Negative
P5	Plasma	Positive
P6	Plasma	Positive

P7	Plasma	Negative
P8	Plasma	Negative
P9	Plasma	Positive
P10	Plasma	Negative
P11	Plasma	Positive
P12	Plasma	Positive
P13	Plasma	Positive
P14	Plasma	Positive
P15	Plasma	Negative
P16	Plasma	Negative
P17	Plasma	Negative
P18	Plasma	Positive
P19	Plasma	Positive
P20	Plasma	Negative

Table 2

#	Type	Status
1	Plasma	Positive
2	Plasma	Positive
3	Plasma	Positive
4	Plasma	Positive
5	Plasma	Positive
6	Plasma	Positive
7	Plasma	Positive
8	Plasma	Positive
9	Plasma	Positive
10	Plasma	Positive
11	Plasma	Positive
12	Plasma	Negative
13	Plasma	Negative
14	Plasma	Negative
15	Plasma	Negative
16	Plasma	Negative
17	Plasma	Negative
18	Plasma	Negative
19	Plasma	Negative
20	Plasma	Negative